REMARKS

The present response is intended to be fully responsive to all points of objection and/or rejection raised by the Examiner and is believed to place the application in condition for allowance. Favorable reconsideration and allowance of the application is respectfully requested.

Status of Claims

Claims 48-53 and 55-60 were pending in the application. Claims 48-53 and 55-60 have been rejected. Claims 48 and 55 have herein been amended.

Claims 50-53 and 57-60 have herein been canceled without prejudice or disclaimer. In making this cancellation without prejudice, Applicants reserve all rights in these claims to file divisional and/or continuation patent applications.

The Telephone Interview

Initially, Applicants wish to thank the Examiner, Examiner Sarvamangala DEVI, for granting and attending the telephone interview, with Applicants' Representative, on February 29, 2006. In the interview, Applicants' draft Response was discussed.

CLAIM REJECTIONS

35 U.S.C. § 112, First Paragraph Rejections

In the Office Action, the Examiner rejected claims 48-53 and 55-60 under 35 U.S.C. § 112, first paragraph, as allegedly containing new subject matter that was not sufficiently described in the specification. The Examiner alleged that the limitations "a plurality of *Neisseria meningitidis* immunotypes" and "said *Neisseria meningitidis* immunotypes selected from the group consisting of L1, L3, L7, L8, L9, L10, L11, and L12" in claims 48 and 55 lack descriptive support in the subject application as filed, because the application allegedly fails to show that an immunogenic composition comprising an inner core of any meningococcal or non-meningococcal Neisseria LPS, wherein a PEtN moiety is linked to

position 3 of the HepII moiety, elicits an antibody against selectively just 2, but not the rest of the named immunotypes.

In response, in order to expedite prosecution, Applicants have amended claims 48 and 55 to overcome the Examiner's rejections.

Applicants therefore respectfully request that the rejection be withdrawn.

Further, the Examiner alleged that the limitations "a plurality of *Neisseria meningitidis* immunotypes" and "said *Neisseria meningitidis* immunotypes selected from the group consisting of L1, L3, L7, L8, L9, L10, L11, and L12" lack descriptive support in the subject application as filed, because the application allegedly fails to show that an immunogenic composition comprising an inner core of any meningococcal or non-meningococcal Neisseria LPS, wherein a PEtN moiety is linked to position 3 of the HepII moiety, elicits an antibody against the *Neisseria meningitidis* (NM) immunotypes L1, L3, L7, L8, L9, L10, L11, and L12.

The Examiner further alleged that the description in the subject specification is limited to a method of eliciting a monoclonal antibody, MAb B5, by administering an immunogenic composition comprising formalin-killed whole cells of a galE NM mutant. The Examiner admitted, however, that the elicited antibody recognized NM immunotypes L1, L3, L7, L8, L9, L10, L11, and L12.

In response, Applicants agree with the Examiner's admission that the elicited antibody recognized the named immunotypes, but respectfully disagree with the rejection.

Contrary to the Examiner's assertions, the disclosure of the subject specification is **not** limited to elicitation of MAb B5. **MAb B5 was used in the experiments presented in the subject application merely as a tool** to define the conserved epitope of the present invention. Accordingly, elicitation of MAb B5 is not an integral part of the methods demonstrated in the subject specification; rather, the subject specification shows that **any antibody elicted by the conserved epitope will recognize other all *Neisseria* strains containing the conserved epitope**, as will be demonstrated.

To support the above point, the subject specification unequivocally shows that:

a. Antibody B5 recognized all tested *Neisseria* strains containing PEtN at this position, but not those strains lacking PEtN at this position, as admitted by the Examiner.

b. Three collections of meningococcal strains -- 153 distinct strains with geographically diverse origins, spanning a period of more than 40 years, representing disease isolates and all LPS immunotypes -- were tested for B5 reactivity. The epitope was present in over 70% of strains and in all LPS immunotypes with PEtN on the 3 position of the Hep2 (L1, L3, L7, L8, L9, L10, L11, or L12), while other immunotypes did not (p. 31-33 and Table 1 of the subject specification). The experiments **were not limited to *Neisseria meningitidis*, but rather utilized several other *Neisseria* species**. These findings provide irrefutable evidence of the requirement for PEtN on the 3 position of the Hep2 as a necessary condition for B5 binding. Clearly, B5 reactivity defines an epitope that is **present and accessible in a wide variety of meningococcal and non-meningococcal *Neisseria* strains, both capsule-deficient and fully encapsulated**. Accessibility of the epitope was further confirmed by immunofluorescence studies (pages 51 and 58-59).

c. To further support the above points, the subject application discloses the structural analysis of the conserved epitope using LPS mutants (page 29), silver stained gels (page 32 and Figure 6), ELISA (page 29), electrospray ionization mass spectrometry (pages 24 and 29), and molecular modeling (page 52).

Thus, the preponderance of evidence presented in the subject application shows that **the presence of a PEtN moiety linked to position 3 of HepII of a Neisseria inner core LPS defines an epitope that is (a) present and conserved; and (b) accessible on all *Neisseria* strains containing PEtN at position 3 of HepII.**

The subject application also shows that:

d. Antibodies elicited by the recited epitope were opsonic and bactericidal and passively protected subjects against *Neisseria meningitidis* infection (pages 56-58).

e. NM immunotypes L1, L3, L7, L8, L9, L10, L11, and L12 contain PEtN linked to position 3 of HepII. (page 31, second full paragraph)

At the time of filing of the subject application, vaccine immunologists at the time of filing of the subject application had **widely accepted** the principles that **(a) if a conserved, accessible epitope is present on an immunogenic composition, the composition will elicit antibodies against pathogens containing the conserved epitope; and (b) elicitation of protective antibodies by the epitope shows that administration of the immunogenic composition will protect against the pathogens containing the conserved epitope**. These principles were so well accepted in the field that **reactivity with protective antibodies against conserved epitopes was used as the criterion to identify synthetic mimetic peptides useful in vaccination**, even though the mimetic peptides had **no other resemblance** to the pathogenic organism. For example, the Chargelegue reference, attached hereto, which was published in March 1998, before the filing date of the subject application, used reactivity with the protective monoclonal antibody MAb 19 to screen the peptide library:

> "In the work described in this paper, a solid-phase combinatorial **peptide library was used to identify peptides that mimic the epitope recognized by this neutralizing and protective MAb**. When used as an immunogen, one of these mimotopes induced virus-neutralizing antibody responses and reduced viral load following challenge of mice with RSV" (paragraph beginning on page 2043; emphasis added; also see first paragraph of Materials and Methods section, p. 2041, and in caption to Table 1, p. 2042)
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> "It is important to note that the sequences identified by this type of approach **do not necessarily have any similarity to the primary amino acid sequence of the F protein of RSV**, but they mimic the conformation of the epitope" (paragraph beginning on page 2044; emphasis added).

In summary, a person skilled in the art would have accepted that the subject application credibly taught the existence of an epitope that is (a) defined by a PEtN moiety linked to position 3 of HepII of the inner core LPS, (b) conserved, (c) accessible, and (d) able to elicit antibodies, and further credibly taught that the conserved epitope is present on NM immunotypes L1, L3, L7, L8, L9, L10, L11, and L12. Thus, a person skilled in the art would

have known that the presence of the conserved epitope recited in the subject claims in an immunogenic composition would be sufficient to elicit antibodies that recognize the *N. meningitidis* immunotypes recited in the subject claims. Accordingly, a person of average skill in the art would have reasonable expectation, based on the subject specification, that **any *Neisseria* strain having a PEtN moiety linked to position 3 of HepII of the inner core LPS can be used to elicit antibodies that recognize NM immunotypes L1, L3, L7, L8, L9, L10, L11, and L12**, as recited in the subject claim.

Thus, the methods recited in the subject claims are sufficiently described and enabled by the subject specification.

Moreover, the Examiner has admitted that the above line of reasoning was accepted by those skilled in the art at the time of filing of the subject application, as evidenced by the Examiner's rejection of the subject claims under 35 U.S.C. § 102 as allegedly anticipated by the Plested et al reference (section 13, pages 6-7 of the Office Action; described in more detail below in the section traversing the rejection). Specifically, the Examiner alleged that, based on the demonstration by Plested that a conserved, accessible epitope is present both on the prior art composition and on *N. meningitidis* immunotypes L1, L3, L7, L8, L9, L10, L11, and L12, the prior art composition would have been expected by a person skilled in the art to elicit antibodies that recognized these *N. meningitidis* immunotypes. Thus, ***the Examiner admitted that those skilled in the art knew at the time of filing of the subject application that, if a conserved, accessible epitope is present on an immunogenic composition, the composition will elicit antibodies against pathogens containing the conserved epitope.*** Accordingly, based on the Examiner's own admissions about what was known in the art, a person skilled in the art would have known that the presence of the conserved epitope recited in the subject claims in an immunogenic composition would be sufficient to elicit antibodies that recognize the *N. meningitidis* immunotypes recited in the subject claims.

Further, since a reference must be enabling to be used for anticipation under 35 U.S.C. § 102, as stated in the MPEP, Section 2121.01, the use of Plested by the Examiner in a U.S.C. § 102 rejection shows that the Examiner clearly believes that Plested would have ***enabled*** one skilled in the art ***to practice the subject matter of the pending claims. All the data and description found in Plested are also found in the subject specification. Thus, the***

Examiner has in effect admitted that the subject specification enables the subject matter of the pending claims.

Applicants therefore respectfully request that the rejection be withdrawn.

Further, the Examiner alleged that the limitations "three or more," "four or more," and "five or more" in claims 50-52 and 57-59 lack descriptive support in the application as filed, because the application allegedly does not show that an immunogenic composition comprising an inner core of any non-meningococcal Neisseria LPS, wherein a PEtN moiety is linked to position 3 of the HepII moiety, elicits an antibody against selectively just 3, 4, or 5, but not the rest of the named immunotypes. The Examiner admitted, however, that the lower limits of these alleged limitations are 3, 4, and 5, respectively.

In response, in order to expedite prosecution, the amended set of claims does not include claims 50-52 and 57-59.

Applicants therefore respectfully request that the rejection be withdrawn.

In addition, in order to clarify the record, Applicants agree with the Examiner's admission that the lower limits of the above alleged limitations are 3, 4, and 5, respectively, but respectfully disagree with the rejection. The plain language of the phrases "three **or more**," "four **or more**," and "five **or more**" contradicts the Examiner's assertion that the elicited antibody must recognize selectively just 3, 4, or 5 of the named immunotypes. "Three" or "more," for example, means that either 3 or more of the named immunotypes may be recognized by the elicited antibodies. Thus, the Examiner has misconstrued the above alleged limitations.

Further, the Examiner alleged that the phrase "a Neisseria LPS" recited in the last line of claims 48 and 55 is different from "said Neisseria LPS" recited in lines 5 and 6 of these claims.

In response, in order to expedite prosecution, Applicants have amended claims 48 and 55 to correct the typographical error.

Applicants therefore respectfully request that the rejection be withdrawn.

35 U.S.C. § 112, Second Paragraph Rejections

Further, the Examiner rejected claims 48-53 and 55-60 under 35 U.S.C. § 112, second paragraph, as allegedly failing to particularly point out and distinctly claim the subject matter regarded as the invention.

The Examiner alleged that the limitation "said inner core of a Neisseria LPS" in claims 48 and 55 appears to lack proper antecedent basis

In response, in order to expedite prosecution, Applicants have corrected the typographical error in claims 48 and 55. Applicants therefore respectfully request that the rejection be withdrawn.

Further, the Examiner alleged that the limitation "said plurality of *Neisseria* immunotypes" near the beginning of claims 50-52 and 57-60 appears to lack proper antecedent basis, and is inconsistent with the phrase "said *Neisseria meningitidis* immunotypes" near the end of the claims.

In response, in order to expedite prosecution, the amended set of claims does not include claims 50-52 and 57-59. Applicants therefore respectfully request that the rejection be withdrawn.

Further, the Examiner alleged that claims 57, 58, and 59 are confusing in scope, because they contain the alleged limitations "wherein said plurality of *Neisseria* immunotypes comprises...or more of said *Neisseria meningitidis* immunotypes."

In response, in order to expedite prosecution, the amended set of claims does not include claims 57-59. Applicants therefore respectfully request that the rejection be withdrawn.

Further, the Examiner alleged that claims 55 and 60 are confusing with regard to their scope, because claim 60 contains the limitations "said plurality of... immunotypes comprises all of said...immunotypes." Thus, it is unclear to the Examiner how claim 60 further limits

claim 60, which includes the alleged limitation "each of a plurality of...immunotypes, said...immunotypes selected from the group consisting of L1, L3, L7, L8, L9, L10, L11, and L12."

In response, in order to expedite prosecution, the amended set of claims does not include claim 60. Applicants therefore respectfully request that the rejection be withdrawn.

Further, the Examiner rejected claims 49-53 and 56-60 because of the alleged indefiniteness in the respective independent claims.

In response, in view of the traversal of the rejections of the independent claims under 35 U.S.C. § 112, second paragraph, Applicants respectfully request that the rejection be withdrawn.

35 U.S.C. § 102 Rejection

Further, the Examiner rejected claims 48-53 and 55-60 under 35 U.S.C. § 102(b), as being anticipated by the Plested et al reference (Infect Immun. 1999 Oct; 67(10): 5417-26). The Examiner alleged (section 13, pages 6-7 of the Office Action) that Plested taught (a) a method of eliciting B5 monoclonal antibody that is specific to LPS inner core, comprising administering to mice an immunogenic composition comprising formalin-killed whole cells of a group B *N. meningitidis* L3 immunotype that comprises the LPS inner core; (b) that the inner core LPS contains an epitope recognized by the monoclonal antibody, B5 and is characterized by the presence of a PEtN moiety linked to the 3' position at HepII of the inner core..; (c) that the inner core LPS in the composition consists of an inner core LPS attached to lipid A and has the formula depicted in Figure 1a of the subject specification; (d) that B5 specifically recognized *N. meningitidis* immunotypes L1, L3, L7, L8, L9, L10, L11, and L12; (e) and that B5 is opsonic. In summary, the Examiner alleged that, based on the demonstration by Plested that a conserved, accessible epitope is present both on the prior art composition and on *N. meningitidis* immunotypes L1, L3, L7, L8, L9, L10, L11, and L12, the prior art composition would have been expected by a person skilled in the art to elicit antibodies that recognized these *N. meningitidis* immunotypes.

Further, the Examiner refused to grant priority to the subject claims from U.S. Provisional Applications 60/196,305, filed 4/12/00, and 60/156,940, filed 09/30/99, alleging that the subject claims contain new matter, and thus lack descriptive support in Provisional Applications 60/196,305 and 60/156,940. Thus, Plested was used as a prior art reference under 35 U.S.C. § 102(b).

In response, in order to expedite prosecution, Applicant have amended claims 48 and 55 to overcome the Examiner's rejections. Applicants therefore respectfully request that the subject claims be granted priority from U.S. Provisional Applications 60/196,305, filed 4/12/00, and 60/156,940, filed 09/30/99, and therefore respectfully request that the rejection under 35 U.S.C. § 102(b) be withdrawn.

In addition, in order to clarify the record, Applicants assert that the amended claims are adequately supported and described in U.S. Provisional Application 60/156,940, which shows, using the same data, that:

a. Antibody B5 recognized all tested *Neisseria* strains containing PEtN at this position, but not those strains lacking PEtN at this position, as admitted by the Examiner (page 16, lines 7-9 of U.S. Provisional Application 60/156,940).

b. B5 reactivity defines an epitope that is present, conserved and accessible in a wide variety of meningococcal and non-meningococcal *Neisseria* strains (lines 1-3 of the first full paragraph on page 18 of U.S. Provisional Application 60/156,940).

c. To further support the above points, U.S. Provisional Application 60/156,940 discloses the structural analysis of the conserved epitope using LPS mutants (page 13), silver stained gels (page 17 and Figure 6), ELISA (page 14), electrospray ionization mass spectrometry (pages 7 and 13), and molecular modeling (p. 52).

As described above in the discussion of the 35 U.S.C. § 112, first paragraph rejections, vaccine immunologists at the time of filing of the subject application had widely accepted the principles that (a) if a conserved, accessible epitope is present on an immunogenic composition, the composition will elicit antibodies against pathogens containing the conserved epitope; and (b) elicitation of protective antibodies by the epitope

shows that administration of the immunogenic composition will protect against the pathogens containing the conserved epitope. Accordingly, a person of average skill in the art would have reasonable expectation, based on U.S. Provisional Application 60/156,940, that **any *Neisseria* strain having a PEtN moiety linked to position 3 of HepII of the inner core LPS can be used to elicit antibodies that recognize NM immunotypes L1, L3, L7, L8, L9, L10, L11, and L12**.

In addition, U.S. Provisional Application 60/196,305 further elaborates upon the findings of Provisional Application 60/156,940.

Thus, the methods recited in the subject claims were sufficiently described and enabled by U.S. Provisional Application 60/156,940 and U.S. Provisional Application 60/196,305.

Moreover, the Examiner's allegations are self-contradictory. The Examiner has alleged that, based on the demonstration by Plested that a conserved, accessible epitope is present both on the prior art composition and on *N. meningitidis* immunotypes L1, L3, L7, L8, L9, L10, L11, and L12, the prior art composition would have been expected by a person skilled in the art to elicit antibodies that recognized these *N. meningitidis* immunotypes. Thus, the Examiner admitted that those skilled in the art knew at the time of filing of the subject application that, if a conserved, accessible epitope is present on an immunogenic composition, the composition will elicit antibodies against pathogens containing the conserved epitope. As described above, U.S. Provisional Application 60/156,940 credibly taught the existence of an epitope that is (a) defined by a PEtN moiety linked to position 3 of HepII of the inner core LPS, (b) conserved, (c) accessible, and (d) able to elicit antibodies, and further credibly taught that the conserved epitope is present on NM immunotypes L1, L3, L7, L8, L9, L10, L11, and L12. Accordingly, based on the Examiner's own admissions about what was known in the art, a person skilled in the art would have known that the presence of the conserved epitope recited in the subject claims in an immunogenic composition would be sufficient to elicit antibodies that recognize the *N. meningitidis* immunotypes recited in the subject claims. Consequently, a person of average skill in the art would have reasonable expectation, based on U.S. Provisional Application 60/156,940, that **any *Neisseria* strain having a PEtN moiety linked to position 3 of HepII of the inner core LPS can be used to**

elicit antibodies that recognize NM immunotypes L1, L3, L7, L8, L9, L10, L11, and L12, as recited in the subject claims.

Thus, the methods recited in the subject claims were sufficiently described and enabled by U.S. Provisional Application 60/156,940 and U.S. Provisional Application 60/196,305.

Further, since a reference must be enabling to be used for anticipation under 35 U.S.C. § 102, as stated in the MPEP, Section 2121.01, the use of Plested by the Examiner in a U.S.C. § 102 rejection shows that the Examiner clearly believes that Plested would have ***enabled*** one skilled in the art ***to practice the subject matter of the pending claims***. Plested contains the ***same data*** as Provisional Application 60/156,940. Thus, the Examiner ***has in effect admitted that Provisional Application 60/156,940 enables the subject matter of the pending claims***.

Since the new claims are supported by U.S. Provisional Applications 60/196,305 and 60/156,940, Applicants respectfully request that the Examiner grant claims of the subject application a priority of U.S. Provisional Applications 60/196,305 and 60/156,940, and consequently, withdraw the rejection under 35 U.S.C. § 102(b).

In view of the foregoing amendments and remarks, the pending claims are deemed to be allowable. Their favorable reconsideration and allowance is respectfully requested.

Should the Examiner have any question or comment as to the form, content or entry of this Amendment, the Examiner is requested to contact the undersigned at the telephone number below. Similarly, if there are any further issues yet to be resolved to advance the prosecution of this application to issue, the Examiner is requested to telephone the undersigned counsel.

Please charge any fees associated with this paper to deposit account No. 50-3355.

Respectfully submitted,

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Dated: March 1, 2006

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